INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2004/002039

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7: C12Q 1/04; G01N 33/574; A61K 47/42

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

IPC 7: C12Q 1/04; G01N 33/574; A61K 47/42

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)

Canadian Patent Database, Pubmed, Delphion, STN; Keywords: chemotherapy, drug resistance, cross resistance, cancer, breast cancer, tumour, taxane, paclitaxel, anthracycline, adriamycin, doxorubicin, DOX, cytotoxic, MCF 7, caspase 9, P-gp, HL-60, PA-1, treatment

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No(s).
X	ROSS DD. et al. "Atypical Multidrug Resistance: Breast Cancer Resistance Protein Messenger RNA Expression In Mitoxantrone-Selected Cell Lines", 03 March 1999 JOURNAL OF THE NATIONAL CANCER INSTITUTE, vol. 91, no. 5, pages 429-433 table 1, page 430	12-14 and 18
X	DEVARAJAN E. et al., "Human Breast Cancer MCF-7 Cell Line Contains Inherently Drug-Resistant Subclones with Distinct Genotypic and Phenotypic Features", May 2002, INTERNATIONAL JOURNAL OF ONCOLOGY, vol. 20, no. 5., pages 913-920 whole document	12-14 and 18

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents.
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 April 2005 (22-04-2005)	05 May 2005 (05-05-2005)
Name and mailing address of the ISA/CA *Canadian Intellectual Property Office* *Place du Portage I, C114 - 1st Floor, Box PCT* *50 Victoria Street* *Gatineau, Quebec K1A 0C9* Facsimile No: 001(819)953-2476	Authorized officer Nicole Harris (819) 997-4541

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International application No.
PCT/CA2004/002039

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No(s).
X	VOLK EL. et al. "Methotrexate Cross-Resistance in a Mitoxantrone-selected Multidrug-resistant MCF7 Breast Cancer Cell Line Is Attributed to Enhance Energy-dependent Drug Efflux", 01 July 2000, CANCER RESEARCH, vol. 60, pages 3514-3520 see page 3516	12-14
Y		1-5, 8-11 and 15-17
X	LITMAN T. et al. "The Multidrug-Resistant Phenotype Associated with Overexpression of the New ABC Half-Transporter, MXR (ABCG2)", June 2000, JOURNAL OF CELL SCIENCE, vol. 113, pages 2011-2021 see whole document	12-14
Y		1-3, 5, 8-11 and 15-17
Y	CA2369303 DANA-FARBER CANCER INS. (Li YZ. et al.), 19 October 2000, see page 26	1-5, 8-11 and 15-17
X	WU GS. et al. "Caspase 9 is Required for p53-Dependent Apoptosis and Chemosensitivity in a Human Ovarian Cancer Cell Line", 3 January 2002, ONCOGENE, vol. 21, no. 1, pages 1-8 whole document	6 and 7
P, X	GUO B. et al. "Potent killing of Paclitaxel and Doxorubicin-Resistant Breast Cancer Cells by Calphostin C Accompanied by Cytoplasmic Vacuolization", November 2003, BREAST CANCER RESEARCH AND TREATMENT, vol. 82, no. 2, pages 125-141 whole document	12-14 and 18

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2004/002039

C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No(s)
P, Y	PARK SJ. et al. "A P-Glycoprotein and MRP1-Independent Doxorubicin-Resistant Variant of the MCF-7 Breast Cancer Cell Line with Defects in Caspase-6, -7, -8, -9 and -10 Activation Pathways", January-February 2004, ANTICANCER RESEARCH, vol. 24, no. 1, pages 123-131 whole document	6 and 7
P, A	FLOROS KV. et al. "mRNA Expression Analysis of a Variety of Apoptosis-Related Genes, Including the Novel Gene of the BCL2-Family, BCL2L12, in HL-60 Leukemia Cells After Treatment with Carboplatin and Doxorubicin", November 2004, BIOLOGICAL CHEMISTRY, vol. 385, no. 11, pages 1099-1103 whole document	6 and 7
A	WU CH. et al. "Beta(2)-Microglobulin Induces Apoptosis in HL-60 Human Leukemia cell Line and its Multidrug Resistant Variants Overexpressing MRP1 but Lacking Bax or Overexpressing P-glycoprotein", 25 October 2001, ONCOGENE, vol. 20, no. 48, pages 7006-7020 whole document	6 and 7
A	MINKO T. et al. "Preliminary Evaluation of Caspase-Dependent Apoptosis Signalling Pathways of Free and HPMA Copolymer-Bound Doxorubicin in Human Ovarian Carcinoma Cells", 28 April 2001, JOURNAL OF CONTROLLED RELEASE, vol. 71, no. 3, pages 227-237 whole document	6 and 7

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons :

1. [ ] Claim Nos. :

because they relate to subject matter not required to be searched by this Authority, namely :

2. [ ] Claim Nos. :

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :

3. [ ] Claim Nos. :

because they are dependant claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows :

Group 1: Claims 1-5, 8-11, 15-17 are directed towards methods using isogenic cell lines for determining the sequence of use of chemotherapeutic, cytotoxic or candidate drugs for killing cancer cells in a patient to reduce the induction of drug cross-resistance. Claims 12-14 and 18 are directed to panels of isogenic cell lines used to carry out said methods.

Group 2: Claims 6 and 7 are directed towards the use and detection of caspase 9 and procaspase 9 to improve the effectiveness of anthracycline drugs in patients resistant to anthracycline drugs

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. [X] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos. :
4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos. :

Remark on Protest [ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/CA2004/002039

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
CA2369303	19-10-2000	EP1181013 A1	27-02-2002
		JP2002541200T T	03-12-2002
		US6664288 B1	16-12-2003
		US2004087610 A1	06-05-2004
		WO0061142 A1	19-10-2000